A Review of Several Studies of Coarse Particulate Matter and Mortality Effects

This review discusses several studies relied upon to demonstrate a causal relationship between coarse PM in the ambient air and mortality. It should be read in conjunction with the accompanying cover letter that explains its scope and supplements its analysis. It concludes that non of these studies demonstrate a probable or significant association between PM10-2.5 and mortality effects that would be a reasonable basis for adopting an ambient standard for coarse particulate matter, much less a basis for establishing a causal relationship. It also outlines observations from a recent article by Brunekreef and Forsberg et al. (2005) that surveys much of the available literature on associations between coarse particulate matter and health effects, and puts it in perspective. Finally, the independent review of the Final Staff Paper by Dr. Jonathan Borak of Yale University Medical School is attached..

1. Ostro, et al.(2000), Coarse and Fine Particles and Daily Mortality in the Coachella Valley, CA: a follow-up study. J. Exposure Anal. Environ.Epidemiol. 10:412-419 (Ostro 2000); Ostro, et al. (2003), Coarse Particles and Daily Mortality in Coachella Valley, California. In: Revised analyses of time-series studies of air pollution and health. Special Report, Health Effects Institute (2003); pp.199-204 (Ostro 2003).

Ostro 2000 studied the relationship between PM10-2.5 and other pollutants and mortality in the Coachella Valley, California, where geologic particles were said to comprise approximately 60% of PM10. Ten years of PM10 data were available, but only 2.5 years of PM10-2.5 data. *No association was found between cardiovascular mortality and PM2.5, between any size of particulate matter and respiratory-related mortality, or between total mortality and PM10-2.5.* However, the authors concluded that the data indicated associations between cardiovascular-specific mortality and both PM10 and PM10-2.5, contrary to the conclusion of the Six Cities Study (see below), and most other studies. This study does not represent the weight of the evidence, nor any central tendency or direction. To the contrary, it is an anomalous study whose findings, at odds with most authority, puzzle its authors, and should not be used as a basis for adopting a coarse particulate standard because:

- Only 2.5 years of PM10-2.5 and PM2.5 data were available, compared to the 10 years of PM10 data. Therefore, in order to obtain a full 10 years of PM10-2.5 data, the authors *extrapolated and estimated PM10-2.5 from PM10 data for the remaining 7.5 years*, using statistical estimating methods. Therefore, three-quarters of the PM10-2.5 data on which the authors relied was not actual measured data. Ostro 2000 at 413; letter from Dr. Jonathan Borak to Ms. Rogene Henderson, Chair of CASAC, dated August 10, 2005 (Borak) at 6-7.

- The correlation between PM10 and PM10-2.5 was high. Dr. Borak notes that this was not surprising, given that PM 10-2.5 was based on and estimated from PM10 using ordinary least squares. He further noted, however, that there was such a poor fit for PM2.5 data that 10-

year estimates for PM2.5 could not be made. This led him to observe that "[i]t is disturbing that this study relied on estimated data that could not fit the expected simple relationship: PM10-2.5 = PM10 – PM2.5.

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[I]t is difficult to accept that the predictive equation truthfully reflects the nature of PM in the Coachella Valley. In turn, *inferences drawn from these estimate data should be viewed with skepticism.*" Borak at 7 (emphasis added). Normally, coarse and fine PM are not highly correlated in arid western areas. Conditions that cause earthen materials to become airborne, such as wind and activity, resulting in high levels of coarse PM are generally dispersive of combustion or fine PM.

- Anomalously, for days of highest PM10 and PM10-2.5 concentrations, the association with daily mortality was less strong. Ostro 2000 at 417.

- It is difficult to understand how Ostro 2000 could have found an association between PM10-2.5 and mortality, but no association between PM2.5 and mortality. This contradicts results in other studies. EPA staff noted that "[t]he CD [Criteria Document] found that evidence from health studies on associations between short-term exposure to PM10-2.5 and mortality was 'not as strong' as evidence for associations with PM2.5 or PM10 but nonetheless was *suggestive* of associations with mortality (CD, p.9-32)" Final SP at 5-49 (emphasis added). In the subsequent reanalysis of the data, using corrected modeling criteria, the authors noted that their results "differ markedly from those of Schwartz et al (1996), who reported associations with fine, but not coarse, mortality in 6 cities." Ostro 2003, at 203.

- Because of the limited years and data for PM10-2.5 and PM2.5, the data for the Coachella Valley was found by EPA to have insufficient precision to be included in the quantitative risk assessment. Final Staff Paper, at 4-6, 4-7; Borak at 7.

- The Staff Paper, Second Draft (January, 2005), concluded that, based on the two studies purporting to find an association between PM10-2.5 and mortality,(Ostro 2000 being one of the two) ***"the evidence associating mortality with short-term exposures to PM10-2.5 is too uncertain to infer a likely causal relationship, although it is suggestive of a possible causal relationship."*** At 5-68 (emphasis added). In the Final Staff Paper, however, the quoted passage was deleted. Neither the data nor the study reports had changed, so as to support a probable association—the only thing that changed was the way in which staff characterized them.

In summary, the conclusions of Ostro, et al regarding the purported association between PM10-2.5 and cardiovascular mortality are questionable because three quarters of the CPM data on which they are based was extrapolated data rather than empirical data; because, anomalously, the days on which the highest CPM concentrations were measured or estimated did not correspond with the highest mortality; because EPA staff found the study to have insufficient precision to be used for purposes of risk assessment; because results showing associations between mortality and PM10-2.5, but not PM2.5, contradict other studies and EPA staff's own analysis, which have found stronger associations between mortality and PM2.5 than with PM10-2.5; and because EPA staff itself found in January (but did not repeat in June) that evidence from this study and the Mar, et al study, discussed *infra at* 3-5, to be too uncertain to infer a causal relationship between PM10-2.5 and mortality.

2. Mar et al. (2000), Association between Air Pollution and Mortality in Phoenix, 1995-1997, Environ. Health Perspectives 108:347-353 (Mar et al. 2000); and Mar, et al.,(2003), Associations Between Air Pollution and Mortality in Phoenix, 1995-1997. In: Revised analyses of time-series studies of air pollution and health. Special report. Health Effects Institute, pp.177-182 (Mar 2003)

Mar 2000 evaluated the association between various particulate matter fractions and various gaseous pollutants, and total and cardiovascular mortality in Phoenix, Arizona, using three years of daily data. Associations between PM10 and total mortality and between PM10-2.5 and total mortality "were "marginal" ($p<0.10$)". Mar 2000, at 350 "Total mortality was not significantly associated with PM2.5". *Id.* Cardiovascular mortality showed a more consistent association with particulate mass concentrations than total mortality, but that association was weakest for PM10-2.5, compared to PM10 and PM2.5. *Id.* Reasons why this study does not show a necessity to regulate coarse PM to protect public health include:

- The fact, as noted, that associations with total mortality were "marginal" and that of all associations between particulate fractions and cardiovascular mortality, the association with PM10-2.5 was "weakest."

- Dr. Borak notes that the lack of significant association between PM2.5 and total mortality is "surprising and difficult to reconcile with the robust associations documented in most studies (and described in the CD). That finding does not seem adequately explained by merely observing that Phoenix PM2.5 represented only a minority of total PM10. In other cities where PM10-2.5>PM2.5 (e.g., Topeka in the Harvard Six Cities Study (citation omitted)), the expected positive association between PM2.5 and mortality was observed.

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"Thus, the lack of an association between PM2.5 and total mortality in Phoenix raises concerns about the integrity of the database and whether it is appropriate as the basis for generalization." Borak, at 5.

- Dr. Borak also notes that, although PM10-2.5 was well correlated with soil (r=0.66), a negative association was found between soil and total mortality and that the Factor Analysis "reported a significant negative association between 'fine soils' and total mortality; there was no significant association between 'fine soil' and cardiovascular mortality.

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"While it is unlikely that exposure to crustal particulate is protective, these findings support the results of other studies (e.g.[Schwartz, 1999]) that found few or no adverse health effects attributable to coarse crustal particulate." Borak, pp. 5-6.

- Dr. Borak opines that "[i]t is unfortunate that this study used only single-pollutant models. [i.e., adjustments were not made to account for confounding effects of other pollutants]. . . . In my earlier letter [of May 4, 2005, to CASAC] I discussed (with respect to the Toronto . . . and Detroit . . . studies) the limitations that stem from use of such models. Based on their study, which found apparent associations with particulates disappeared after adjustment for co-pollutants, Burnett and colleagues recommended that:

  'all available air pollution measures be considered in assessing the effects of any single pollutant on health.' (citation omitted)

  Likewise, the HEI Health Research Committee echoed that recommendation in its comments on the Detroit study:

  'In order to determine the relative effects of several risk factors on a health outcome, ideally all variables under consideration would be included in a single model.' (citation omitted)

  The use of single-pollutant models limits the meaningfulness of the conclusions drawn from the Phoenix study." Borak at 6.

- As noted above, the Second Draft of the Staff Paper (modified in the final version), stated, in connection with the Ostro and Mar studies that "*the evidence associating mortality with short-term exposures to PM10-2.5 is too uncertain to infer a likely causal relationship, although it is suggestive of a possible causal relationship.*" At 5-68 (emphasis added).

In summary, the Phoenix study is of marginal value because it reflects only a marginal association between total mortality and PM10-2.5 and, of the various fractions

of particulate matter, the weakest association between cardiovascular mortality and PM10-2.5; it contradicts the prevailing scientific consensus that the association between mortality and PM2.5 is stronger than that between mortality and PM10-2.5; it anomalously shows no significant association between soil and cardiovascular mortality (and a negative association between soil and total mortality) even though soil is 66% of PM10-2.5; it fails to adjust for the potentially confounding effects of co-pollutants; and EPA Staff found in January 2005 that the evidence of the Mar and Ostro studies was too uncertain to show a probable association between PM10-2.5 and mortality.

3. Schwartz, et al. (1996) Is Daily Mortality Associated Specifically with Fine Particles? Air & Waste Manage. Assoc. 46:927-939 (Schwartz et al. 1996); Klemm and Mason (2003), Replication of Reanalysis of Harvard Six-City Mortality Study. In: Revised analyses of time-series studies of air pollution and health. Special Report, Health Effects Institute (2003), pp. 165-172 (Klemm 2003).
Schwartz 1996 did a reanalysis of data from the Harvard Six-Cities Study to determine, primarily, whether the associations between particulate air pollution and daily mortality were specifically due to fine particles. Data for coarse particulate matter also were analyzed. The Final SP states that "a statistically significant association was reported between PM10-2.5 and mortality in Steubenville" as part of the Schwartz analysis. Final SP at 5-63. The Steubenville data suffer from limitations explicitly noted by EPA Staff. More importantly, Schwartz 1996 does **not** conclude that there was a significant association between PM10-2.5 and mortality in Steubenville, and directly contradicts the conclusion stated by Staff.

- EPA staff itself discounted the Steubenville data as imprecise, and on that basis excluded Steubenville from the quantitative risk assessment. Final SP at 4-6; Borak at 8.

- Most importantly, the conclusion regarding PM10-2.5 and Steubenville in Schwartz 1999 contradicts the characterization found in the final SP. Although Schwartz initially did show an apparent association between PM10-2.5 and mortality in Steubenville (an association not found in any of the other five cities studied), further analysis revealed that this apparent association "was explained by PM 2.5," and that "*it is likely that Steubenville PM10-2.5 data were confounded by PM2.5.*"" Borak at 8 (emphasis added). In Steubenville, unlike the other cities, there was a high correlation between PM2.5 and PM10-2.5. Schwartz 1996 at 930 and 931, Table 4. Analysis of the data showed that the "estimated effect of a 10 μg/m3 increase in CM[PM10-2.5] would increase proportionately with the correlation between CM and PM2.5." Schwartz 1996 at 934 and Figure 3. *"This suggests that the association is with exposure to fine particles . . ." Id.* (emphasis added). Dr. Borak adds that "it seems very likely that the apparent association of mortality and coarse particulate in Steubenville was due to unresolved confounding." Borak at 9. Thus, contrary to the Final SP, the Steubenville data is consistent with the conclusion for all the six cities stated by Schwartz et al., namely: "The particle associations were

specifically with fine particle mass concentrations, with little additional contributions from the coarse particle mass fraction. . . . **For the coarse particle mass fraction, the combined effect estimate was weaker, not statistically significant, and inconsistent in the city-specific associations. In regression analyses including both PM2.5 and CM, the estimated associations with PM2.5 was unaffected while the CM association became effectively zero.**" Schwartz 1996 at 934.(Emphasis added.)

- "It is also noteworthy that in one of the six cities (Topeka) there was a negative association between mortality and PM10-2.5 (but not PM2.5). Topeka was also the only city for which PM10-2.5 levels > PM2.5 levels. These findings suggest that in Topeka, a city 'subject to windblown dust', coarse particulate was predominantly crustal and therefore associated with a negative exposure-effect relationship." Borak at 9. As noted by Dr. Borak regarding a similar negative association with soil in Phoenix, "[w]hile it is unlikely that exposure to crustal particulate is protective, these findings support the results of other studies (citation omitted) that found few or no adverse health effects attributable to coarse particulate." Borak at 6.

Thus, contrary to EPA Staff's perspective, Schwartz 1996 does not conclude that there was a significant association between PM10-2.5 and mortality in Steubenville.

4. Sheppard, et al. (1999), Effects of Ambient Air Pollution on Nonelderly Asthma Hospital Admissions in Seattle, Washington, 1987-1994, Epidemiology 10:23-30 (Sheppard 1999); Sheppard (2003), Ambient Air Pollution and Nonelderly Asthma Hospital Admissions in Seattle, Washington, 1987-1994, In: Revised analyses of time-series studies of air pollution and health. Special Report, Health Effects Institute; pp. 2278-230 (Sheppard 2003)

The Sheppard studies in Seattle did not investigate mortality effects, but only morbidity effects—the association between various pollutants and nonelderly hospital admissions for asthma. The Final SP cites Ostro, Mar and the Six Cities Steubenville data as reporting associations between PM10-2.5 and mortality, but it does not cite Sheppard for any mortality association. The purported associations between asthma admissions and PM10-2.5 concentrations that are discussed by Sheppard were critiqued by the NCBA in its March 21. 2005 comments to CASAC on the Second Draft Staff Paper, and by Dr. Borak in his May 4, 2005 comments to CASAC on behalf of the NCBA. Those critiques note, among other things, that for particulate matter, there was data missing for a huge number of days in the study period. The PM2.5 data necessary to calculate PM10-2.5 were missing on 72% and 84%, respectively, of the days in the study period at the two monitoring sites where both PM10 and PM2.5 were monitored. Therefore Sheppard's results for particulate matter associations with asthma admissions were based primarily on imputed data. Most importantly for our purposes in this paper, however, Sheppard had no data at all regarding mortality.

5. Brunekreef and Forsberg (2005), Epidemiological evidence of effects of coarse airborne particles on health, European Respiratory Journal, 26:309-318. (Brunekreef)

Brunekreef surveyed all available epidemiological studies on the health effects of coarse particles. It is instructive to note a few of the observations made regarding studies of effects of coarse particles on short-term mortality effects.

- There are four studies that reported results of a two-pollutant analysis, where adjustments were made for possible confounding effects as between fine and coarse particulate matter. Three of the four "found that effects of coarse PM were no longer there after adjustment for fine PM, whereas the fine PM effects remained." Brunekreef at 310. "Only a study from Mexico City found the opposite result. The authors speculated that there was much biogenic contamination in the coarse fraction in Mexico City." *Id.*

- Of the studies reporting only single pollutant analyses (remember that single pollutant models fail to account for potential confounding effects of co-pollutants, *supra* at 4-5) Schwartz 1996, "**the study with the largest number of observation, some 190,000 deaths observed over a number of years" found that fine PM was associated with morality but coarse PM was not.**" *Id.* 9 (emphasis added). A Philadelphia study found associations of similar magnitude between mortality and fine and coarse PM, "although the associations with CM were mostly not significant." *Id.* The EPA Criteria Document calculated effect estimates in the order of a 1.6% increase in cardiovascular mortality per 10 $\mu g/m^3$ for both metrics, "being significant for fine but not for coarse." *Id.*at 10-11. "A number of studies [five] found no evidence of effects of either PM metric on mortality." *Id.* "In Santiago, coarse PM were more important than FP in summer." *Id* at 311.

- Brunekreef cites the Ostro and Mar studies in the Coachella Valley and Phoenix, respectively. As to Ostro, it is noted that there was evidence of effects of fine particles on total mortality, but not coarse particles, and "[w]hen the analysis was restricted to cardiovascular mortality, there was a significant association with coarse but not fine particles, although the effect estimate for fine particles was still much larger than for coarse PM." *Id.* As to Mar, it is noted that coarse PM is higher than fine PM in Phoenix, that both were found to be associated with cardiovascular mortality at lag 0, and that at lag 1 the association was stronger for fine than for coarse particles. *Id.*

Brunekreef helps to put the Ostro and Mar studies in perspective. These studies show apparent associations between coarse particulate matter and cardiovascular-

specific mortality. It is important, however, to note both the limitations and anomalies in these studies, as discussed above, and the fact that their conclusions regarding coarse particles run counter to the substantial weight of the evidence in the scientific literature. As EPA staff noted in the Second Draft of the Staff Paper, "the evidence associating mortality with short-term exposures to PM10-2.5 is too uncertain to infer a likely causal relationship, although it is suggestive of a possible causal relationship." At 5-68. The suggestion of a possible association between coarse particles and mortality certainly supports the need for further study. We submit that, considering all the evidence, it cannot support the adoption of a coarse particle standard at this time.

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